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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,833	07/16/2007	Markus Wimmer	2579.022US1	3319

21186 7590 09/07/2010

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EXAMINER
BECKHARDT, LYNDSEY MARIE

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
09/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/591,833	WIMMER ET AL.	
	Examiner	Art Unit	
	LYNDSEY BECKHARDT	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16 and 18-23* is/are pending in the application.

4a) Of the above claim(s) *1-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-13,16 and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/05/2006 and 10/28/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13, 16 and 18-23 are currently pending. Claims 9-13, 16 and 18-23 are currently under examination.

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on 06/15/2010 is acknowledged. Applicant has stated the election was with traverse, however has presented to reasons for the traversal.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/15/2010.

It is noted that Applicant stated 'Applicant's respectfully cancel claims 1-8, 14 and 16 (Group I)" in the reply filed 06/15/2010, however claims 1-8 were presented in the claims filed 06/15/2010. Thus the claims are being withdrawn, as drawn to the non-elected invention.

Applicant's election of lubricin and hyaluronic acid in the reply filed on 06/15/2010 is acknowledged. The species election is hereby withdrawn in view of Applicant's amendment's submitted 06/15/2010.

Priority

The instant application claims priority to PCT/CH04/00131, filed 03/05/2004.

Information Disclosure Statement

Applicant's Informational Disclosure Statements, filed on 09/05/2010 and 10/28/2008 have been considered. Please refer to Applicant's copy of the 1449 submitted herein.

New Matter

Claims 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 22 and 23 are directed to 'lubricin to hyaluronic acid ranges from 0.02 to 0.05% by weight' and '0.2 to 0.4%' by weight. The instant specification does not provide support for a combination of lubricin to hyaluronic acid in the claimed range. The instant specification discloses substances of Group A in the ranges of 0.02 to 0.05% by weight and Group B ranges from 0.2 to .4% weight, however this is different than the instant claims 22 and 23 are directed to. Applicant is required to cancel the claims or point where support is found in the instant specification.

Claim Rejections - 35 USC § 112- first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 and dependent claims 10-13 and 18-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 9 recites the limitation, “derivatives of these substances” in references lubricin and hyaluronic acid. Applicant has not described the claimed genus of "derivatatives" in a manner that would indicate they were in possession of the full scope of this genus, or even to describe what this genus is comprised of.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." Eli Lilly, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description

requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter aria*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although Eli Lilly and Enzo were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. Univ. of Rochester v. G.D. Searle & Co., 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

In the instant case, the claims are drawn to a method for the production of a natural cartilage replacement material, comprising dissolving in a solvent lubricin and hyaluronic acid and derivatives of these substances. Applicants described no "derivatives of these substances" other than mentioning in the specification “a mixture of one or several substances from group A) ….with one of several substances from group B)…. and derivatives of said substances” (abstract). While lubricin and hyaluronic acid are disclosed, there is no disclosure of any so-called derivatives thereof. No derivatives are described in such as way as to allow one skilled in the art to ascertain that Applicant is in possession of the entire scope of the claimed genus. Applicants have not described this genus in a manner that would allow one skilled in the art to immediately envisage the compounds contemplated for use. As such, the claims lack adequate written description for the myriad of compounds embraced by the claimed "derivatives of these substances” referring to lubricin and hyaluronic acid.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 recites the limitation "said mixture" in the third line. There is insufficient antecedent basis for this limitation in the claim. Claim 9, from which claim 10 depends, has been amended and no longer in includes a 'mixture'.

Claims 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what 'lubricin to hyaluronic acid ranges

from 0.02 to 0.05% by weight' and '0.2 to 0.4%' by weight is regarding. Further support in the instant specification cannot be found to clarify the issue, see new matter rejection above. Support for lubricin (group A) in the range of 0.02 to 0.05% and hyaluronic acid (group b) in the range of 0.2 to 0.4% by weight has been found in the instant specification (page 5, paragraph [0023]). With respect to prior art claim 22 will be interpreted as being directed to lubricin in the range of 0.02% to 0.05%. With respect to prior art, claim 23 will be directed to hyaluronic acid in the range of 0.2 to 0.4%. Applicant is asked to clarify claims 22-23.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grad (applicant provided on IDS dated 09/05/2006) in view of US 5,702,456 (patent date: 12/30/1997) and US 5,891,558 (patent date: 04/06/1999).

Grad teaches a growing body of evidence indicates that physiological stresses and strains in and around the cells are crucial for generating functional tissue in vitro. In particular, chrondocyte activity is stimulated by the mechanical demands made on the environment. A cartilage engineering bioreactor has been developed that provides joint specific biomechanical stimuli (page 797, second column, last paragraph). The study investigated the effect of axial compression and surface motion on chondrocytes seeded onto biodegradable scaffolds, with particular emphasis on the expression of SZP/lubricin, which is known to play a key role in maintaining a functional articular surface and joint lubrication (page 798, first column, first paragraph). Cylindrical porous polyurethane scaffolds were seeded with bovine articular chondrocytes and subjected to static or dynamic compression with and without surface motion, which was accomplished by rotation of a ceramic hip and ball over the construct surface (page 798, first column, second paragraph). The results indicate that reciprocating sliding is a

potent modulator of SZP/lubricin expression. Applied surface motion may therefore be considered for engineering cartilage like constructs with a functional surface and lubrication properties (page 798, first column fourth paragraph).

Grad does not teach dissolving in a solvent lubricin and hyaluronic acid.

The '456 patent teaches a total joint orthopedic implant (abstract). A step for establishing a boundary lubricant layer on the total joint implant surfaces is taught. This is done by including a boundary lubricant layer forming solutes in the fluid bath. The solutes may for example be selected from the group of materials consisting of polytetrafluoroethylene, hyaluronic acid, lubricin and other natural or synthetic solvents or solutes and any mixtures thereof (column 4, lines 6-16). The boundary layer forming solutes are absorbed and incorporated into the surface of the joint implant, and particularly in the sliding load bearing surface areas, those solutes are replaced. As a result of lubricant absorption, friction between the wear bearing surfaces is reduced following implantation and the production of troublesome wear particles is thereby further minimized (column 4, lines 20-30).

The '558 patent teaches foams which may be used in tissue repair and reconstruction (abstract). Cartilage implants are taught (column 16, lines 51-53). The foam is taught to be seeded with chondrocytes (column 16, lines 61-63). A mechanical device is taught to be used which placed the biopolymer foam containing the chondrocytes into gentle contact with a second surface, e.g. a second biopolymer foam containing chondrocytes, in the presence of fluid having similar characteristics as those of synovial fluid and which contains hyaluronic acid which is thixotropic fluid, i.e., a gel

which liquefies when agitated but which reverts to a gel upon standing. The biopolymer foam coating the chondrocytes and the second surface are then rotated or slid across one another to create shear and compressive forces which mimic those which cartilage tissue is exposed in vivo. The resulting cartilage tissue ahs the properties of normal artiuclar cartilage tissue, e.g. the ability and architecture to withstand forces to which normally cartilage tissue is exposed (column 17, lines 12-27).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use a mixture of hyaluronic acid and lubricin in view of the teaches of the ‘456 patent on the cartilage construct taught by Grad because Grad teaches the desire for increased lubricin for surface lubrication and the '456 patent teaches application of a mixture of hyaluronic acid and lubricin to establish a boundary lubricant layer. One of ordinary skill in the art at the time the invention was made would have a high expectation of success in using the mixture of hyaluronic acid and lubricin on the cartilage implant taught by Grad because Grad teaches the desire for more lubricin and the ‘456 publication teaches a coating layer of lubricin and hyaluronic acid on an implantable material and the ‘558 patent teaches hyaluronic acid is found in synovial fluid and used in contact with cartilage replacing implants.

Regarding claims 9 and 16, Grad teaches a cartilage like construct with the desire for lubricin for its lubricating properties. The '456 patent teaches a solution containing a mixture of lubricin and hyaluronic acid.

Regarding claim 10, Grad teaches a porous polyurethane scaffold was seeded with chondrocytes. The ‘456 patent teaches submersion of an implant in a solution of hyaluronic acid and lubricin.

Regarding claim 11, the ‘558 patent teaches a solution containing hyaluronic acid brought in contact with a cartilage replacing implant by sliding across one another. It would be prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sliding force taught by the '558 patent to bring cartilage implant taught by Grad and the solution taught by the ‘456 in contact because the ‘558 patent teaches a rotation and sliding to contact the hyaluronic acid containing solution and Grad teaches surface motion and rotation being applied to the cartilage construct.

Regarding claims 12 and 13, Grad teaches cylindrical porous polyurethane scaffolds were seeded with bovine articular chondrocytes and subjected to static or dynamic compression with and without surface motion, which was accomplished by rotation of a ceramic hip and ball over the construct surface.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grad (applicant provided on IDS dated 09/05/2006), US 5,702,456 (patent date: 12/30/1997) and US 5,891,558 (patent date: 04/06/1999) as applied to claims 9-13 and 16 above, and further in view of US 2003/0211992 (publication date: 11/13/2003).

As mentioned in the above 103(a) rejection, all the limitations of claims 9-13 and 16 are taught by the combination of Grad, the '456 patent and the '558 patent. The combination of references does not teach the solvent being Ringer solution.

The '992 patent teaches a method for the treatment of cartilage disorders (abstract). Generally, the formulations are prepared by contacting the analog or peptide uniformity and intimately with liquid carriers. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood or synovial fluid of the recipient. Examples include Ringer's solution (pages 15-16, paragraph [0175]).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use Ringer solution as the solvent in the hyaluronic acid lubricin mixture as taught by the combination of Grad, the '456 patent and the '558 patent because Ringer's solution is taught to be isotonic with synovial fluid and used in cartilage treating formulations and the '558 patent teaches the hyaluronic acid solution to be like synovial fluid.

Claims 18-20 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grad (applicant provided on IDS dated 09/05/2006), US 5,702,456 (patent date: 12/30/1997) and US 5,891,558 (patent date: 04/06/1999) as applied to claims 9-13 and 16 above, and further in view of US 5,432,167 (patent date: 07/11/1995), US 5,171,273 (patent date: 12/15/1992) and Olsen (publication date: 10/01/2002).

As mentioned in the above 103(a) rejection, all the limitations of claims 9-13 and 16 are taught by the combination of Grad, the '456 patent and the '558 patent. The combination of references does not teach the ratio of lubricin to hyaluronic acid or the molecular weight of hyaluronic acid.

The '167 patent teaches a cell proliferation matrix consisting of an aqueous gel of hyaluronic acid (abstract). The gel is taught to contain 0.1 to 2% hyaluronic acid with an average molecular weight of at least 25,000 DA. The average molecular weight of sodium hyaluronate to be used in the invention is suitable in the range of 1.2×10^6 to 2.5×10^6 (column 2, lines 3-15). It should be understood that the aqueous gel according to the invention should have a viscosity which allows the hyaluronic acid or salt thereof to be in a dissolved state, so that the molecules can easily function in the matrix. If the concentration exceeds 2.0 percent then the viscosity of the gel is probably too high. On the other hand, if the concentration of the sodium hyaluronate is less than 0.1% by weight of the aqueous gel, then the gel will probably be too diluted for the gel to stay in place when applied (column 2, lines 18-30).

The '273 patent teaches implants (abstract). The implant is taught to be a scaffold which is replaced by maturing tissue (column 7, lines 23-40). The implant fibers are taught to be immersed in a proteoglycan solution (column 9, lines 1-5). Proteoglycan from cartilage are taught as desirable (column 10, lines 5-13). The proteoglycan is taught to not exceed about one percent by weight (column 28, claim 6).

Olsen teaches lubricin is also known as proteoglycan 4 (page 14, last paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use hyaluronic acid in the range of 0.01% to 2% as taught by the '167 patent for the hyaluronic acid gel taught by the combination of Grad, the '456 patent and the '588 patent because the '167 patent teaches the viscosity of the hyaluronic acid gel can be controlled by the percent in the solution in order for the gel to stay in place when applied to an implant. One of ordinary skill in the art would have had a high expectation of success in using the hyaluronic acid in the percents taught by the '167 patent because the '167 patent teaches a cell proliferation implant and the combination of references are directed to a cartilage replacement scaffold containing chondrocytes. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use lubricin at a concentration of less than 1% because the '273 patent teaches the use of less than 1% proteoglycan for scaffold implants wherein the proteoglycan is from cartilage and Olsen teaches lubricin is known as proteoglycan. One of ordinary skill in the art at the time the invention was made would be motivated to use a percent of lubricin that is known to be used in combination with scaffold implants, such as is taught by the combination of the '273 patent and Olsen.

Regarding claim 18, the '167 patent teaches the average molecular weight of hyaluronic acid is in the range of 1.2×10^6 to 2.5×10^6.

Regarding claims 19-20, the '167 patent teaches the use of between 0.01% and 2% hyaluronic acid. The '273 patent and Olsen teach the use of less than 1% lubricin. It would be prima facie obvious to one of ordinary skill in the art at the time the invention

was made to optimize the amount of lubricin and hyaluronic acid in the mixture in order to obtain the desired properties, such as viscosity and lubrication, through routine experimentation. MPEP 2144.05 recites "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine optimization".

Regarding claim 22, the '273 patent teaches proteoglycan solutions being below 1%. As MPEP 2144.05 recites "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine optimization". See 112 second paragraph rejection for claim interpretation above.

Regarding claim 23, the '167 patent teaches the use of hyaluronic acid in the range of 0.01% to 2%. See 112 second paragraph rejection for claim interpretation above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYNDSEY BECKHARDT whose telephone number is (571)270-7676. The examiner can normally be reached on Monday thru Thursday 7:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LYNDSEY BECKHARDT/
Examiner, Art Unit 1613

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